

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
LAURA A. CORUZZI  
JONES DAY  
222 EAST 41ST STREET  
NEW YORK, NY 10017-6702

## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 10589-41-228		Date of mailing (day/month/year) <b>24 APR 2007</b> <b>FOR FURTHER ACTION</b> See paragraph 2 below
International application No. PCT/US04/21334	International filing date (day/month/year) 02 July 2004 (02.07.2004)	Priority date (day/month/year) 02 July 2003 (02.07.2003)
International Patent Classification (IPC) or both national classification and IPC IPC: Please See Continuation Sheet USPC: 435/196,320.1,69.1,325,252.3,19;536/23.2,23.5;530/350		
Applicant PTC THERAPEUTICS, INC.		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I      Basis of the opinion
- ☐ Box No. II      Priority
- ☒ Box No. III      Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV      Lack of unity of invention
- ☒ Box No. V      Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI      Certain documents cited
- ☐ Box No. VII      Certain defects in the international application
- ☐ Box No. VIII      Certain observations on the international application

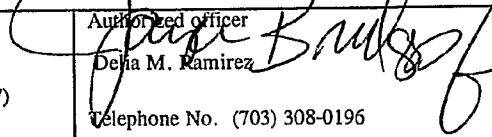
### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Date of completion of this opinion 10 April 2007 (10.04.2007)	Authorized officer  Deha M. Ramirez Telephone No. (703) 308-0196
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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

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**Box No. I Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
- ☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☒ a sequence listing
- ☐ table(s) related to the sequence listing

b. format of material

- ☒ on paper
- ☒ in electronic form

c. time of filing/furnishing

- ☒ contained in the international application as filed.
- ☒ filed together with the international application in electronic form.
- ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 1-20,36,37 and 39-90

because:

☐ the said international application, or the said claim Nos. \_\_\_\_\_ relate to the following subject matter which does not require an international search (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_ are so unclear that no meaningful opinion could be formed (*specify*):

☒ the claims, or said claims Nos. 1-20,36,37 and 39-90 are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

Please See Continuation Sheet

☐ no international search report has been established for said claims Nos. \_\_\_\_\_

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

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**Box No. IV Lack of unity of invention**

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has, within the applicable time limit:
- ☐ paid additional fees
  - ☐ paid additional fees under protest and, where applicable, the protest fee
  - ☐ paid additional fees under protest but the applicable protest fee was not paid
  - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
  - ☒ not complied with for the following reasons:  
See the lack of unity section of the International Search Report (Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:
- ☐ all parts.
  - ☒ the parts relating to claims Nos. 21-33

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**Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Claims <u>21-23, 30-31</u>	YES
	Claims <u>24-29, 32-33</u>	NO
Inventive step (IS)	Claims <u>21-23</u>	YES
	Claims <u>24-33</u>	NO
Industrial applicability (IA)	Claims <u>21-33</u>	YES
	Claims <u>NONE</u>	NO

**2. Citations and explanations:**

Claims 24-29 lack novelty under PCT Article 33(2) as being anticipated by Strausberg, R., (GenBank accession number BC019582, 03 January 2002). Strausberg teaches a nucleic acid which is longer than the polynucleotide of SEQ ID NO: 11 that comprises all of SEQ ID NO: 11 except that it contains a segment of 51 nucleotides between nucleotides 907-908 of SEQ ID NO: 11. Strausberg, R. also teaches a vector comprising the nucleic acid (pCMV-SPORT6) and a cell comprising the vector (*E. coli* DH10B). Claims 24-29 are directed to a nucleic acid which would hybridize under highly stringent conditions to the nucleic acid of SEQ ID NO: 11, vectors comprising the nucleic acid, and host cells comprising the vector. Since the nucleic acid of Strausberg, R. would hybridize to the polynucleotide of SEQ ID NO: 11 under the conditions recited, the teachings of Strausberg, R., anticipate the instant claims as written.

Claims 32-33 lack novelty under PCT Article 33(2) as being anticipated by Strausberg, R., (GenBank accession number AAH19582, 03 January 2002). Strausberg teaches a protein which is longer than the polypeptide of SEQ ID NO: 12 that comprises all of SEQ ID NO: 12 except that it contains a segment of 17 amino acids between residues 303-304 of SEQ ID NO: 12. The polypeptide of Strausberg, R. is encoded by a nucleic acid which comprises all of SEQ ID NO: 11 except that it contains a segment of 51 nucleotides between nucleotides 907-908 of SEQ ID NO: 11 (GenBank accession number BC019582, 03 January 2002). Claims 32-33 are directed to a protein encoded by a nucleic acid which would hybridize under highly stringent conditions to the nucleic acid of SEQ ID NO: 11. Since the polynucleotide encoding the polypeptide of Strausberg, R., would hybridize to the nucleic acid of SEQ ID NO: 11 under the stringent conditions recited, the teachings of Strausberg, R., anticipate the instant claims as written.

Claims 30-31 lack an inventive step under PCT Article 33(3) as being obvious over Strausberg, R., (GenBank accession number BC019582, 03 January 2002). The teachings of Strausberg, R. have been discussed above. Strausberg does not teach a method to recombinantly produce the polypeptide. Claims 30-31 are directed in part to a method to recombinantly produce a polypeptide encoded by a nucleic acid which would hybridize under highly stringent conditions to the nucleic acid of SEQ ID NO: 11. It would have been obvious to one of ordinary skill in the art to recombinantly produce the polypeptide of Strausberg by transforming a host cell with an expression vector comprising the nucleic acid encoding the polypeptide of Strausberg. One of ordinary skill in the art is motivated to construct such vector, transform a host cell and produce the protein recombinantly for the benefit of producing sufficient amounts of the protein for further characterization in a consistent fashion. There is reasonable expectation of success at recombinantly producing the polypeptide of Strausberg because construction of expression vectors, transformation of host cells with such vectors, and expression of the desired protein in a recombinant host cell are well known and widely used in the art. Therefore, the invention as a whole would have been *prima facie* obvious over the prior art.

Claims 21-23 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the polynucleotide of SEQ ID NO: 11, the polypeptide of SEQ ID NO: 12, or a polypeptide comprising amino acids 280-330 of SEQ ID NO: 12.

Claims 21-33 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

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**Supplemental Box**

In case the space in any of the preceding boxes is not sufficient.

Continuation of IPC:

C12N 9/16( 2006.01),15/00( 2006.01),5/10( 2006.01),1/20( 2006.01);C12P 21/06( 2006.01);C07H 21/04( 2006.01);C07K 14/00( 2006.01)

C12Q 1/44( 2006.01)

**Section III. Non-establishment of opinion (claims inadequately supported by description)**

Claims 1-20, 36-37, 39-90 were found not examinable because the sequences associated with the accession numbers as recited in the claims cannot be search as they are not associated with a sequence identifier in compliance with sequence rules. Sequences recited in a claim must have a sequence identifier and be included in a computer readable form for a proper search to be conducted. Also, those sequences in the accession numbers recited can change at any time without notice.